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Oxidation of Diphenyl Diselenide with Ceric Ammonium Nitrate: a Novel Route for Functionalization of Olefins

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Abstract - Alkenes were reacted with diphenyl diselenide in presence of ceric ammonium nitrate in methanol, affording β-methoxyalkyl phenyl selenides in good yields.

Due to its importance, the introduction of phenylseleno group in organic molecules has been widely studied in recent years.[1] To this purpose in addition to PhSeCl and PhSeBr many novel reagents were used, such as phenylselenenic acid,[2] N-phenylselenophtalimide[3] and N-phenylselenosuccinimide.[4]

Particularly, diphenyl diselenide was found to react with several oxidizing agents in presence of alkenes and in various solvents to give β-functionalized alkylphenyl selenides. Ammonium peroxydisulfate showed to be the most effective oxidant of PhSeSePh.[5-9] The mechanism of oxidation is thought to proceed through a single electron transfer (SET) process that produces the radical ion $[PhSeSePh]^{\dot{+}}$ as intermediate, which further evolves into the reactive electrophilic $[PhSe]^+$ species. The successive addition of the latter to olefinic double bond in nucleophilic solvents or in presence of various nucleophiles leads to the synthesis of various classes of organic compounds. Nevertheless, other oxidants were not so effective in the oxidation of PhSeSePh, and the results obtained in the functionalization of most olefins were unsatisfactory. Therefore the finding of new experimental conditions to carry out the oxidation of diphenyl diselenide was a really important target.

Considering the hyphotesis of a SET mechanism operating in the oxidation of diphenyl diselenide by peroxydisulfate, we decided to investigate the reactivity of known SET reagents towards PhSeSePh in methanol in presence of olefins.

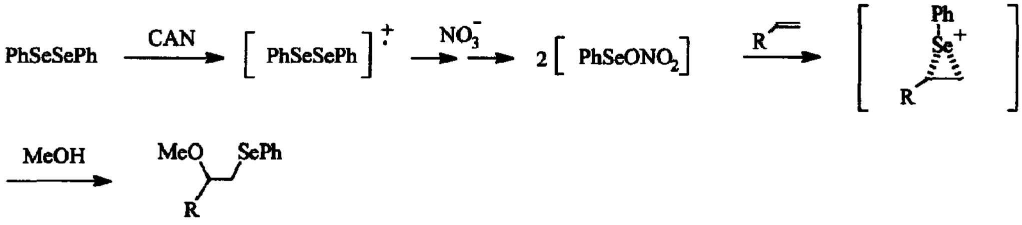
The reagent we chose was ceric ammonium nitrate (CAN) that is known to be a good oxidant in this solvent. First, diphenyl diselenide was treated only with CAN in methanol at room temperature (PhSeSePh and CAN were in a 1:2 molar ratio), showing the disappearance of the former in few hours.

The formation of not isolable polar selenium species was evidenced by the formation of a spot at Rf = 0 on TLC plate. $PhSeONO_2$ is probably one of the involved species, and the possible path of its formation is depicted in Scheme 1.

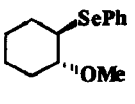
The addition of olefins to this reaction mixture resulted in the formation of β-methoxyalkyl phenylselenides in low to modest yields. On the other hand, when ceric ammonium nitrate was added in one portion to a solution of alkene and PhSeSePh in methanol the reaction showed to be really fast, leading to the synthesis of the expected β-methoxyalkyl phenylselenide.

The best yields in the shortest reaction times were obtained employing alkene, PhSeSePh and CAN in a 1:1:2 molar ratio. Yields markedly diminished when reagents were used in stoichiometric amount (2:1:2 molar ratio). This seems to be due to side oxidation processes of diphenyl diselenide by CAN.

Scheme 1



Results obtained in the methoxylation of various alkenes are summarized in Table 1. Any attempt to improve the yields by increasing the reaction time was unsuccessful.



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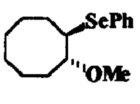

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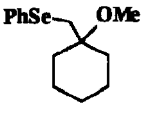

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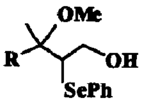
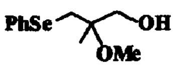


4 R=Me
6 R=H



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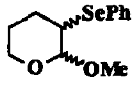

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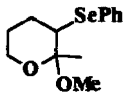

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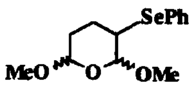

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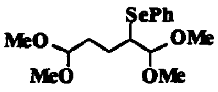

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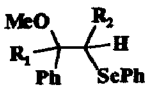


11 $R_1 = R_2 = H$
12 $R_1 = H, R_2 = Ph$
13 $R_1 = Ph, R_2 = H$

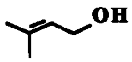
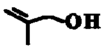
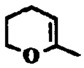
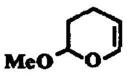
The reaction was highly regioselective when carried out on trisubstituted olefins, activated alkenes (such as phenyl substituted olefins) or enol ethers, always leading to a Markownikoff orientation.

Moreover, the intermediacy of a cationic selenium species was proved by the particular stereochemistry of final products. As a matter of fact the reactions of cyclohexene, cyclooctene and stilbene with CAN and PhSeSePh afforded compounds 1, 2 and 12 respectively, identical to those obtained by reaction of the same alkenes with PhSeCl (known to give *anti* addition products) in methanol.

The use of CAN together with PhSeSePh as selenilating agents is convenient because diphenyl diselenide is cheaper and less toxic than PhSeCl or PhSeBr. Ceric ammonium nitrate showed to be a good oxidant for diphenyl diselenide and the amount of β-methoxyalkyl phenylselenides obtained was dependent on the nature of the olefin we used. Experimental conditions were mild and reactions went to completion in short times.

In most cases yields are comparable to those obtained using ammonium peroxydisulfate as oxidant.[5-9]

Table 1. Reaction of Olefins with CAN and PhSeSePh in Methanol

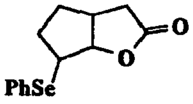
Alkene	Product	Reaction time (hr)	Yields (%)[a]
Cyclohexene	1	0.5	93
Cyclooctene	2	0.5	72
Methylene-cyclohexane	3	0.5	60
	4	3	65
	5	3	50
	6	1.5	97[b]
	7	3	75[c]
	8	14	53
	9	3	39[d]
	10		48
Styrene	11	14	65
trans-Stilbene	12	1.5	80[e]
1,1-Diphenyl-ethylene	13	14	62

a) Yields are referred to isolated, pure products and are calculated on the initial amount of olefin;
b) *Erythro/threo* mixture; c) *cis/trans* mixture; d) Diastereomeric mixture; e) *Erythro* form

In a typical experimental procedure, 2.0 mmoles of alkene were placed in 30 ml of anhydrous methanol under an argon athmosphere; then, PhSeSePh (630 mg, 2.0 mmoles) and ceric ammonium nitrate (2.20 g, 4.0 mmoles) were added, and the resulting mixture was kept under stirring at room temperature until its orange colour turned in pale yellow or totally disappeared. Water was added and the methanolic fraction was removed under reduced pressure. The residue was extracted with CH_2Cl_2 (3x50 ml) and the organic phase dried over Na_2SO_4; removal of the solvent "in vacuo" afforded an oily residue, which was purified on a silica gel column eluted with light petroleum ether/Et_2O to give pure products.

The use of CAN as an oxidant of diphenyl diselenide is not restricted only to the methoxylation reaction of alkenes. In the experimental conditions above mentioned also alkenes with an internal nucleophile react to give selenilated cyclic compounds.

In this way 2-cyclopentene-1-acetic acid and 5-hexen-2-ol were transformed into the γ-lactonic compound **14** and five-membered cyclic ether **15** in high yields (72% and 83% respectively) and in short reaction times (0.5h).



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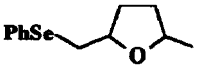

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Starting from these results, this method seems to be very promising and suitable to improve the transformations of olefins already described in literature and carried out with PhSeSePh and other oxidizing agents.

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